Name: #

Pipe Cleaner Protein Modeling

The function of a protein is determined by its shape, and the shape of the protein is determined by its amino acids. Because proteins are smaller than microscopic, we can explore them in an indirect way through modeling.

Everything in science is done with models – the scientific method itself is about modeling complex ideas into simpler formats so that we can better understand them. Scientific models may also help us to do things that would otherwise be impossible. For example, there is no way that we could have sequenced the 6 billion bases in the human genome without prior experience with simpler organisms like nematodes with genomes smaller than our own.

A model is a substitute for the actual thing we are studying, but it is also similar to what it represents. It tends to follow the same rules as the actual object, and it provides us with a simpler idea of a more complex process so that we can better understand it.

In this case, you will be using pipe cleaners, beads, and cut up straws to model how proteins fold, and how mutations affect the shape of proteins. Each person will be responsible for completing their own handout, but you only need to make one normal protein and one mutated protein per group.

**There are 3 basic laws of protein folding:**

1. **Hydrophobicity** – hydrophobic (*water hating*) amino acids will always try to be oriented inside of a protein.
   1. Because our bodies are mostly water, hydrophobic amino acids basically try to ‘hide’ in this kind of environment.
   2. On the other hand, hydrophilic (*water loving*) amino acids try to get further into or closer to the water because they “love” it so much. Hydrophilic amino acids will try to be oriented facing outwards from the center of the protein as close to water they can be.
2. **Charge** – amino acids can have one of three charges – positive, negative, or neutral
   1. Like opposite sides of a magnet, positively and negatively charged amino acids try to move toward each other
   2. Like the same pole of a magnet, amino acids with similar charges (positive and positive, or negative and negative) will try to move as far apart from each other as they can.
   3. Neutral amino acids remain largely unaffected by other “R” groups.
3. **Cysteine** **Bonds** – cysteine amino acids are attracted even more so than charged R groups. Cysteine amino acid pairs will move toward each other and form covalent bonds between their sulfur atoms whenever they can. These are some of the strongest bonds in proteins’ secondary & tertiary structure.

**To represent amino acids, we will use colored beads. Read the “rules” below before getting started.**

1. Hydrophobicity – yellow beads will represent hydrophobic amino acids; pink beads will represent hydrophilic amino acids. As such, all yellow beads should be as far inside the protein as they can, and pink beads should be on the outside whenever possible.
2. Charge – blue beads will be a positive charge and red beads will be the negatively charged amino acids (we won’t bother with neutral amino acids). Red and blue beads near each other should for a bond (if they can); similarly colored blues or reds should be as far apart as possible.
3. Cysteine bonds – we’ll use green to represent the amino acids cysteine; green beads should form pairs whenever they can.
4. Some amino acids may have multiple beads to represent their characteristics. For example, Arginine is both positively charged (blue) and hydrophilic (yellow). As such, you would use both a blue and yellow bead together to represent this amino acid.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity** |  | **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity** |
| Alanine | Ala | A | Neutral | Hydrophobic |  | Leucine | Leu | L | Neutral | Hydrophobic |
| Arginine | Arg | R | **Positive** | *Hydrophilic* |  | Lysine | Lys | K | **Positive** | *Hydrophilic* |
| Asparagine | Asn | N | Neutral | *Hydrophilic* |  | Methionine | Met | M | Neutral | Hydrophobic |
| Aspartic acid | Asp | D | **Negative** | *Hydrophilic* |  | Phenylalanine | Phe | F | Neutral | Hydrophobic |
| Cysteine | Cys | C | Neutral | *Hydrophilic* |  | Proline | Pro | P | Neutral | Hydrophobic |
| Glutamine | Glu | Q | Positive | *Hydrophilic* |  | Serine | Ser | S | Neutral | *Hydrophilic* |
| Glutamic acid | Gln | E | **Negative** | *Hydrophilic* |  | Threonine | Thr | T | Neutral | *Hydrophilic* |
| Glycine | Gly | G | Neutral | Hydrophobic |  | Tryptophan | Trp | W | Neutral | Hydrophobic |
| Histidine | His | H | **Positive** | *Hydrophilic* |  | Tyrosine | Tyr | Y | Neutral | Hydrophobic |
| Isoleucine | Ile | I | Neutral | Hydrophobic |  | Valine | Val | V | Neutral | Hydrophobic |

1. Use a cut up straw in between each amino acid to represent peptide bonds. You may need multiple pipe cleaners to fit all of your amino acids.

**DIRECTIONS for modeling:**

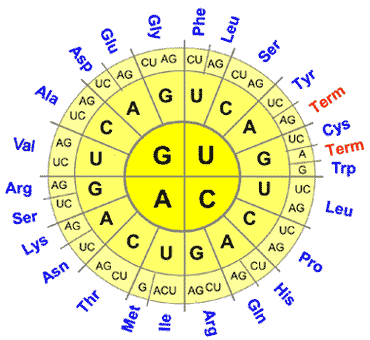
1. You will begin by creating the mRNA strand of a gene (transcription). You have been given the antisense strand, so use *complementary base pairing* rules.
2. From your mRNA strand, you will need to create codons; remember that a codon is a group of 3 bases that codes for a specific amino acid. Your codons are read in the 5’ 🡪 3’
3. You will then need to convert your codons into amino acids in the 5’ 🡪 3’ direction (translation).
4. Once you have your order of amino acids, you will need to find your respective beads and assemble them onto a pipe cleaner. Again, be sure to separate each bead by a cut up straw! (TERM is not an amino acid but a command; it will not have a bead).
5. Finally, you will need to fold your protein. Start by moving your pink to the outside and your yellow to the inside. Then connect your opposite charges and cysteine amino acids (wrap them around each other using the pipe cleaner to represent their bond). Your finished protein should have an ‘outer shell’ of hydrophilic and charged amino acids with an inner center of hydrophobic amino acids.
6. When you are done, you will also have to create a second protein from the same gene which has been mutated.

DNA Strand (the second side of this strand has been omitted for easier reading) with ***start i***dentified:

3’ TAC-TTA-CGA-TGG-TAC-ACG-CAA-TCT-ATA-CTC-AAA-TAT-AGG-ACC-TTG-ACG-TCG-AAT-CTC-CAC-TGT-ACC-TTG-AAC-CTG-ACT 5’

mRNA Strand (written in codons):

5’-AUG- AAU-   
  
   
  
Amino Acid Sequence

MET- ASN -

Now create your protein using the chart below

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity** |  | **Amino Acid** | **Code** |  | **Charge** | **Hydrophobicity** |
| Alanine | Ala | A | Neutral | Hydrophobic |  | Leucine | Leu | L | Neutral | Hydrophobic |
| Arginine | Arg | R | **Positive** | *Hydrophilic* |  | Lysine | Lys | K | **Positive** | *Hydrophilic* |
| Asparagine | Asn | N | Neutral | *Hydrophilic* |  | Methionine | Met | M | Neutral | Hydrophobic |
| Aspartic acid | Asp | D | **Negative** | *Hydrophilic* |  | Phenylalanine | Phe | F | Neutral | Hydrophobic |
| Cysteine | Cys | C | Neutral | *Hydrophilic* |  | Proline | Pro | P | Neutral | Hydrophobic |
| Glutamine | Glu | Q | Positive | *Hydrophilic* |  | Serine | Ser | S | Neutral | *Hydrophilic* |
| Glutamic acid | Gln | E | **Negative** | *Hydrophilic* |  | Threonine | Thr | T | Neutral | *Hydrophilic* |
| Glycine | Gly | G | Neutral | Hydrophobic |  | Tryptophan | Trp | W | Neutral | Hydrophobic |
| Histidine | His | H | **Positive** | *Hydrophilic* |  | Tyrosine | Tyr | Y | Neutral | Hydrophobic |
| Isoleucine | Ile | I | Neutral | Hydrophobic |  | Valine | Val | V | Neutral | Hydrophobic |

Once you have finished your protein, compare yours with your table partner’s. They should look similar. After you’ve gotten your protein approved, create a second, mutated version of your gene by either adding or deleting a base. Write your mutated gene, mRNA, and amino acid sequence below. Then create your mutated protein.

Original DNA

3’ TAC-TTA-CGA-TGG-TAC-ACG-CAA-TCT-ATA-CTC-AAA-TAT-AGG-ACC-TTG-ACG-TCG-AAT-CTC-CAC-TGT-ACC-TTG-AAC-CTG-ACT 5’

Mutated DNA

Mutated mRNA  
  
   
  
   
  
Mutated Amino Acid Sequence  
  
   
  
   
  
   
  
   
Adapted from: